

**REMARKS**

Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

Applicants thank the Examiner for entering the Amendment filed April 22, 2005.

Applicants point out that dMsh2-9 cell lines recited in the claim and specification, not Msh2-9 cell lines, were deposited at ATCC on March 19, 2005. To verify a deposit of dMsh2-9 cell lines, applicants provide a copy of Budapest Treaty Deposit Form indicating that a deposition of the cell line dMsh2-9 under number RH532 was made on March 19, 2005, at ATCC Depository; and a declaration of Stephen B. Maebius, the attorney of record in the above referenced application, stating that the cell lines were deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date May 27, 2005  
FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5569  
Facsimile: (202) 672-5399

By A. Sapigin (Reg. No. 35,439)  
Stephen B. Maebius  
Attorney for Applicant  
Registration No. 35,264  
*Alexey Sapigin*



***IN THE UNITED STATES PATENT AND TRADEMARK OFFICE***

Applicant: Henricus Petrus Joseph TE RIELE et al.  
Title: HOMOLOGOUS RECOMBINATION IN MISMATCH REPAIR  
INACTIVATED EUKARYOTIC CELLS  
Appl. No.: 09/884,877  
Filing Date: 06/20/2001  
Examiner: Joseph T. Voitach  
Art Unit: 1632

**DECLARATION**

Commissioner for Patents  
Washington, D.C. 20231

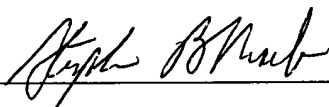
Sir:

I declare:

1. A deposit of the cell line dMsh2-9 under number RH532 was made at the American Type Culture Collection (ATCC), P.O. Box 1548, Manassas, VA 20108, and accepted under the provisions of the Budapest Treaty for patent purposes.
2. The deposit under number RH532 was received by ATCC on March 19, 2005.
3. All restrictions on the availability to the public of the culture deposited will be irrevocably removed upon the granting of a patent from the above-identified application.
4. The deposit will be replaced if viable samples cannot be dispensed by the depository.
5. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so

made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Signed this 26<sup>th</sup> day of May, 2005.

A handwritten signature in cursive script, appearing to read "Stephen B. Maebius", written over a horizontal line.

Name: Stephen B. Maebius  
Reg. No. 35,264  
Applicants' Representative



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**ATCC**<sup>®</sup>

**BUDAPEST TREATY DEPOSIT FORM (BP/1)**

American Type Culture Collection

P.O. Box 1549

Manassas, VA 20108

TO DEPOSIT OR TO CONVERT A DEPOSIT TO MEET THE REQUIREMENTS OF THE BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF A PATENT PROCEDURE

**ALL QUESTIONS MUST BE COMPLETED IN ENGLISH. PLEASE USE ONE FORM FOR EACH STRAIN DEPOSITED.**

1 Name of deposit. Please mark the appropriate box and provide the information requested for the material.

- ☐ Microorganism - the complete scientific name including genus and species plus the source of the material  
☐ Virus - the name, whether plant or animal, and source including geographic location  
☒ Cell line - the species and tissue of origin, geographical source of isolation, and any known associated hazards (HIV, EBV, etc.)  
☐ Genetic material - the name of organism from which vector, clone or library is derived, the source of the DNA insert identified by species (e.g., human, mouse) or scientific name, the name of gene, and the identity of the host organism  
☐ Consortia or mixed culture - the identity of each component of the mixture  
☐ Seeds, embryos, insect eggs, etc. - the common name, the scientific name of the source of the deposit, and geographical source

Mouse embryonic stem cells with a disruption in the Msh2 gene. Genotype: Msh2<sup>-/-</sup>; Name: dMsh2-9

2. Strain designation\* (i.e., number, symbols, etc.) RH532

\*The strain designation must correspond with the vial labels.

3 Is this an original deposit under the Budapest Treaty? ☒ Yes ☐ No

4 Is this a request for a conversion of a deposit already at the ATCC to meet the requirements of the Budapest Treaty?

☐ Yes ☒ No

If yes, please indicate ATCC designation \_\_\_\_\_

5 Is this deposit a mixture of microorganisms or cells? ☐ Yes ☒ No

If yes, please describe. \_\_\_\_\_

6. Provide details necessary to cultivate, test for viability and store the deposit. If a mixture, provide description of components and a method to check for presence. If a plasmid, provide name of host and antibiotic resistance.

Cells can be grown on gelatin-coated tissue-culture surfaces in complete medium +  $\beta$ -mercaptoethanol (0.1 mM) + LIF (10<sup>3</sup> U/ml) (Complete medium = GMEM + 10% FCS + Na-pyruvate 1 mM + non-essential amino acids)

7 Provide sufficient description so that ATCC may confirm deposit properties (e.g., Gram negative rod)

a. If deposit is a cell culture, is it being cultured in the presence of antibiotics? ☐ Yes ☒ No

If yes, please list the antibiotics: \_\_\_\_\_

b. If deposit is a hybridoma, what is the isotype of the antibody produced? \_\_\_\_\_

8. Safety: Is this strain hazardous to humans? NO Animals? NO Plants? NO

If yes, what is the recommended biosafety level for working with this strain? \_\_\_\_\_

(Refer to Biosafety in Microbiological and Biomedical Laboratories, 4th ed. HHS Publication No. (CDC) 93-8385. U.S. Department of Health and Human Services, Centers for Disease Control, Washington, DC. U.S. Government Printing Office, 1999. The entire text is available online at [www.cdc.gov/od/ohs/biosafety/bml4/bml4toc.htm](http://www.cdc.gov/od/ohs/biosafety/bml4/bml4toc.htm).)

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## 9. Regulatory Compliance:

- a. Was the material derived from a human? ☐ Yes ☒ No  
If yes, was an IRB-approved consent form (human subjects) obtained? ☐ Yes ☐ No
- b. Was this material obtained from wildlife? ☐ Yes ☒ No  
If yes, please indicate genus and species and whether wild or captive bred. \_\_\_\_\_
- c. Is work performed at your facility with exotic viruses affecting livestock and avian species? ☐ Yes ☒ No
- d. Identify any reagents of animal origin used to cultivate this organism/cell line (serum, growth factors, trypsin, etc.) and manufacturer, if known: Fetal Calf Serum

## 10. Availability:

Prior to issuance of a U.S. Patent, ATCC will only make a culture available as instructed by the depositor or relevant patent office. Samples must be provided to a specific investigator if a pertinent Patent Office under the Budapest Treaty instructs ATCC to do so. The following questions must be answered:

- a. As of date of deposit or conversion to meet the requirements of the Budapest Treaty, do you wish the deposit to be made available to anyone who requests a culture? If yes, there are no restrictions on distribution. Answering no will ensure the deposit is not available until the patent has issued. ☒ Yes ☐ No
- b. As of the date of deposit or conversion to meet the requirements of the Budapest Treaty, do you wish the deposit to be made available to requesters that satisfy Patent Offices in countries not signatory to the Budapest Treaty? ☒ Yes ☐ No  
If "yes," please state which countries: All

Please note that if you are converting your deposit to meet the requirements of the Budapest Treaty, and your deposit has already been released for distribution due to the issuance of a U.S. Patent, you cannot restrict it from further distribution. After a U.S. Patent issues and we are so notified, ATCC makes the culture available to anyone who requests it, as allowed under U.S. Patent and Trademark Office (USPTO) Rules and Regulations (37 CFR 1.808 (a)(2)).

## 11. Notification. ATCC will notify you of your ATCC number after viability of the deposit has been confirmed.

Name of individual to notify: Hein te Riele  
Fax: 31206691383 Phone: 31205122084 E-mail: h.t.rielle@nki.nl

## 12. Payment by check or credit card (MasterCard, VISA or American Express) must accompany the deposit unless prior arrangements for billing have been made and approved. ATCC accepts purchase orders for the exact amount.

Purchase Order No. \_\_\_\_\_ Check No. \_\_\_\_\_  
Credit Card number \_\_\_\_\_ ☐ MasterCard ☐ VISA ☐ American Express  
Exp. Date \_\_\_\_\_ Name shown on card: \_\_\_\_\_  
(Please print clearly or type)  
Signature of card holder: \_\_\_\_\_

## PAYMENT: ATCC MUST HAVE A BILLING ADDRESS, CONTACT PERSON, PHONE AND FAX FOR ALL DEPOSITS:

Contact Name: \_\_\_\_\_

Billing Address: \_\_\_\_\_

Phone: (\_\_\_\_) \_\_\_\_\_ Fax: (\_\_\_\_) \_\_\_\_\_

Do you have a current ATCC account number? ☐ Yes ☐ No

If Yes, ATCC Account Number is: \_\_\_\_\_

If No: To apply for an account with ATCC, please complete a New Account Application located on our Web site ([www.atcc.org](http://www.atcc.org)) and return it with supporting documentation to ATCC for approval.

USD 2500 has been transferred to ATCC, 007923990752, ADA 052001633  
Cto Bank of America, Baltimore, MD, Federal ID 52-0196548  
by MIXIS France

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13. Name, address, phone and fax number of your Attorney of Record

Prof. dr. Anton Berns, The Netherlands Cancer Institute  
Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands  
P: 31 20 512 1990 (Ref: Docket or Case No. \_\_\_\_\_)  
F: 31 20 512 2011

14. MUST BE COMPLETED. Deposited on behalf of: (Verify with your management who owns the deposit. The owner is usually a company or institution, and not an individual.)

The Netherlands Cancer Institute / Antoni van Leeuwenhoek  
Hospital

I understand and agree that the deposit may not be withdrawn by me for the period specified in Rule 9.1 of the Budapest Treaty (at least 30 years after the date of deposit or 5 years after the date of the most recent request for the deposit, whichever is longer), and that if a culture should die or be destroyed during the life of the patent, or the period of time so specified, it is my responsibility to replace it with a living culture of the same organism or cell. In the cases of viruses, cell cultures, plasmids, embryos, and seeds, it is my responsibility to supply a sufficient quantity for distribution for the period of time specified above.

S. Rodenhuis  
 Printed Name

[Signature]  
 Signature

16/03/05  
 Date

Address: NKTI AVL Plesmanlaan 121 - 1066 CX Amsterdam NL

Phone: (020) 512 2870 Fax: (020) 512 2858 E-mail: srodenu@ukin.nl

## SHIPPING INFORMATION

BEFORE SHIPPING, PLEASE CONTACT THE ATCC PATENT DEPOSITORY FOR SHIPMENT ADVICE:

Fax: (703) 365-2745  
 E-mail: PatentDeposit@atcc.org

## SHIPPING NOTICE:

The depositor is ultimately responsible for the shipment of deposits to ATCC and compliance with all applicable government regulations for the packaging and movement of the material. The depositor shall indemnify ATCC, to the extent permitted by law, against claims resulting from the violation of applicable government regulations caused by the depositor's shipment of deposits to ATCC.

## STORAGE & FEES

**Storage:** Cultures are stored for 30 years from date of deposit or five years after the last request for a sample, whichever is longer, as required under the rules of patent offices in most countries.

**Fees:** All fees are subject to change. For current fees and other information, check our Web site at [www.atcc.org](http://www.atcc.org) or request a quotation of fees by e-mail at PatentDeposit@atcc.org or fax (703) 365-2745.

ATCC USE ONLY; ATCC DESIGNATION \_\_\_\_\_ REC'D \_\_\_\_\_ V.T. RESULT \_\_\_\_\_

ATCC® is a registered trademark of the American Type Culture Collection.